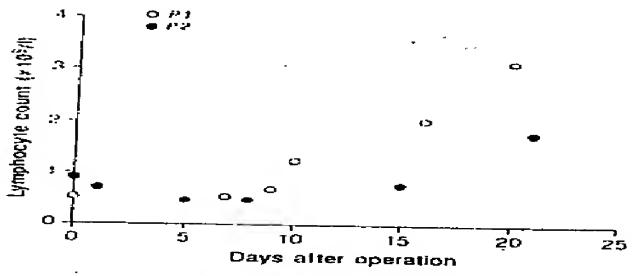


Lymphocyte counts after bowel resection.

blood lymphocyte count in patients with perforated diverticular disease ($p < 0.01$, Tukey test):

Diagnostic group	*n*	*Mean lymphocyte count (95% CI)*
Emergency surgery	6	0·73 (0·39–1·36)
Acute diverticulitis	28	1·16 (0·99–1·36)
Bleeding diverticula	17	1·48 (1·17–1·87)
Quiescent diverticula	10	1·53 (1·18–1·98)

Lymphocyte counts may return to normal ten days after surgery as in patient 1 (figure). All patients were afebrile by the fifth postoperative day. The single exception to this pattern was an individual with multiple inflamed perforated diverticula that were discovered at laparotomy. After initial surgery, he required further resection of necrotic tissue. This patient's lymphocyte count remained below 1×10^9/l for 16 days (P2 in figure). All patients had normal chest radiographs before their operation; thus, lymphopenia was not attributable to adult respiratory distress syndrome, in which there is widespread margination and extravasation of white cells to lung vessels together with extravasation of fluid. Lymphopenia seems to be a reversible component of the disease associated with bowel necrosis, as seen in appendicitis.[1] By contrast, the more global picture of leucopenia in diverticulitis is associated with generalised peritonitis in those cases with high morbidity and mortality.[3] Lymphocytopenia could be secondary to either massive lymphocyte recruitment into an extravascular compartment or systemic effects of bacterial endotoxin and cytokines.[4,5] We believe that the lymphocyte count may be worthy of more attention than it usually receives.

Academic Unit of Surgery,
University College London,
Whittington Hospital,
London N19 5NF, UK; and
ICRF Human Tumour Immunology Group,
University College and Middlesex
School of Medicine

S. R. BAKER
C. A. MICHIE
K. S. SOO
J. H. WYLLIE
P. C. L. BEVERLEY

1. Jahangiri M, Wyllie JH. Peripheral blood lymphopenia in gangrenous appendicitis. *Br Med J* 1990; 301: 215–17.
2. Aparicio PM, Pages MN, Verspaget HW, et al. In vitro cellular cytotoxicity in Crohn's disease and ulcerative colitis: relation with disease activity and treatment, and the effect of recombinant gamma-interferon. *J Clin Lab Immunol* 1989; 29: 119–24.
3. Renier JF, Goeav-Brissonniere O, De-Cervens P, et al. Surgical treatment of perforated diverticular sigmoiditis. A retrospective study apropos of 45 cases. *J Chir Paris* 1989; 126: 567–74.
4. Isselkutz TB, Stoltz JM. Stimulation of lymphocyte migration by endotoxin, tumor necrosis factor and interferon. *Cell Immunol* 1989; 120: 165–73.
5. Kohler PC, Hank JA, Moore KH, Sturmer B, Sondel PM. Phase I clinical trials of recombinant IL2. *Cancer Invest* 1989; 7: 213–23.

Coeliac disease and lymphoma

SIR,—We believe that some of the misunderstanding (Aug 3, p 318) relating to Professor Wright and colleagues' report (June 8, p 1373) results from a failure to distinguish clearly between neoplasia and malignant disease. Two years ago we pointed out that the term "lymphoma" is generally applied to malignant lymphoid tumours but that there are also benign B and T cell neoplasms that have gone unrecognised in the past because the neoplastic cells are mature and morphologically normal and, like their normal counterparts, mingle with other cells without producing sharply defined tumour masses. Unregulated functional activity of such neoplasms can lead to immunopathological disturbances and to histopathological appearances that masquerade as chronic inflammation.[1] The principle may apply to coeliac disease, as we originally suggested.[1] The finding in cells of the relevant clone of chromosomal or molecular abnormalities at the loci of growth-regulating genes would provide further evidence in favour of the T cell neoplasia hypothesis in patients without overt malignant disease.

Department of Pathology,
Royal Infirmary,
Glasgow G4 0SF, UK

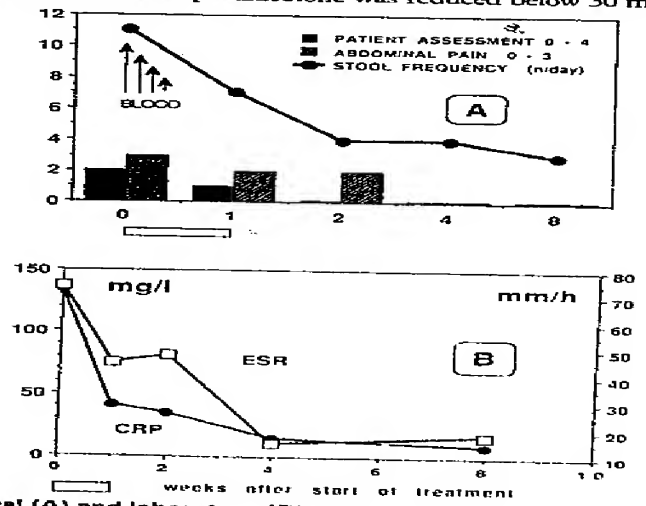
R. B. GOUDIE
F. D. LEE

1. Goudie RB, Lee FD. Does occult monoclonal proliferation of non-malignant T cells cause secondary immunopathological disorders? *J Pathol* 1989; 158: 91–92.

Treatment of inflammatory bowel disease with anti-CD4 monoclonal antibody

SIR,—The aetiology of Crohn's disease and ulcerative colitis is unknown. The efficacy of corticosteroids and immunosuppressive agents suggests a central role for immunological mechanisms in their pathogenesis. The increased expression of class II histocompatibility antigens on colonic enterocytes[1] and considerable lymphocyte activation[2] indicate that the immune system of the gut is hyperreactive in inflammatory bowel disease. The monoclonal antibody (mAb) MAX.16H5 has been used successfully in the treatment of severe rheumatoid arthritis.[3] We have therefore investigated the therapeutic effect of MAX.16H5 directed against the CD4 surface molecule on helper T-cells in 3 patients with chronic active steroid-resistant or steroid-dependent inflammatory bowel disease. Diagnosis of Crohn's disease or ulcerative colitis was based on endoscopic, radiological, and histological criteria. In the present study, a dose of 0·3 mg/kg MAX.16H5 was infused on each of seven consecutive days. 1·5 g (patients 1 and 2) or 3 g (patient 3) mesalazine and 10 mg prednisolone were maintained throughout the observation period.

Patient 1 was a 47-year-old man with a 10-year history of Crohn's disease and extensive perianal fistulae. Previous treatment with sulphasalazine, mesalazine, prednisolone, azathioprine, and metronidazole was ineffective. In the past year, he had had severe flare-ups whenever prednisolone was reduced below 30 mg daily.



Clinical (A) and laboratory (B) data in patient 3 with ulcerative colitis.

Daily infusions of 0·3 mg anti-CD4 mAb (MAX.16H5) per kg body weight for 7 days (open bars).

His Crohn's disease activity index (CDAI)[4] was 177 and systemic indices of inflammation were raised (erythrocyte sedimentation rate [ESR] 67 mm/h, orosomucoids 2·7 g/l, C-reactive protein [CRP] 88·6 mg/l). He improved rapidly, had no pain, and stools were normal for three weeks after anti-CD4 treatment. ESR fell to 45 mm/h, orosomucoids to 1·8 g/l, and CRP to 38 mg/l. After four weeks, he had a mild relapse, which responded to a higher dose of prednisolone (20 mg).

Patients 2 and 3 both had a longstanding history (6 and 9 years, respectively) of severe left-sided ulcerative colitis, with multiple relapses despite appropriate maintenance therapy. Both had had chronically active disease for more than six months. Moderate improvement was only seen at more than 30 mg prednisolone per day. Patient 2 responded to anti-CD4 treatment clinically, and by a transient reduction of CRP, but relapsed after one month. Patient 3, however, has had complete clinical, endoscopic, and biochemical remission (figure) for more than five months.

In inflammatory bowel disease, T cells in the lamina propria may represent an unusual stage of differentiation, and they seem to be hyperresponsive;[5] this might contribute to local inflammation. In our study, treatment with MAX.16H5 led to a substantial and immediate depletion of CD4 cells from the circulation in all patients as has been shown in rheumatoid arthritis.[3] Anti-CD4 treatment also induced striking immunomodulation, as shown by reduced lymphocyte proliferation on stimulation with various mitogens and recall antigens. A transient reduction of the density of CD4 molecules on the surface of helper T cells was also seen. Whether or not these observations are part of the mechanism of action of this therapy is unknown. It is noteworthy that CD4 depletion could be detected to the same extent and with the same kinetics in both responders and non-responders to anti-CD4 therapy who had rheumatoid arthritis.[3]

None of our patients had side-effects from antibody treatment. Our findings demonstrate that such therapy can be successful in inflammatory bowel disease when conventional drugs have failed. A single cycle of anti-CD4 at the doses we used is not sufficient to persistently suppress disease activity in all patients. Prolonged or repeated courses of antibody therapy or in combination with immunosuppressive drugs should be considered.

The Max-Planck-Research Unit for Rheumatology/Immunology is funded by the German Ministry for Research and Technology (BMFT).

Medical Clinic,
and Institute of Clinical Immunology,
University of Rostock,
D-2500 Rostock, Germany
J. EMMRICH
M. SEYFARTH

Medical Clinic I, and Clinical Research
Unit for Rheumatology/Immunology,
Institute for Immunology,
University of Erlangen-Nürnberg,
University of Erlangen,
D-8520 Erlangen, Germany
W. E. FLEIG
F. EMMRICH

1. Selby WS, Janossy G, Mason DY, Jewell DP. Expression of HLA-DR antigens by colonic epithelium in inflammatory bowel disease. *Clin Exp Immunol* 1983; 53: 614–18.
2. Raedler A, Fraenkel S, Klese G, Thiele HG. Elevated numbers of peripheral T cell in inflammatory bowel diseases displaying T9 antigen and Fc alpha receptors. *Clin Exp Immunol* 1985; 60: 518–24.
3. Horneff G, Burmester GR, Emmrich F, Kalden JR. Treatment of rheumatoid arthritis with an anti-CD4 monoclonal antibody. *Arthritis Rheumatism* 1991; 34: 129–40.
4. Best WR, Becktel JM, Singleton JW, Kern F Jr. Development of a Crohn's disease activity index. *Gastroenterology* 1976; 70: 439–44.
5. Zeitz M, Quinn TC, Graeff AS, James SP. Mucosal T cells provide helper function but do not proliferate when stimulated by specific antigen in Lymphogranuloma venerum proctitis in nonhuman primates. *Gastroenterology* 1988; 94: 353–66.

Pancreatitis associated with *Salmonella* enteritis

SIR,—After the letter from Dr Renner and colleagues (June 29, p 1611), who suggest that pancreatitis is common in salmonellosis, we describe our own experience. We have recently completed a retrospective review of all 343 adults admitted to our hospital with non-typhoidal salmonella gastroenteritis between January, 1982, and June, 1989. The commonest isolates were *Salmonella typhimurium* (44·5%) and *S enteritidis* (27·6%); 27 (17·1%) of the 158 patients who had blood cultures taken were bacteraemic. Complications were noted, but serum amylase estimations and abdominal ultrasonography were rarely completed and were not systematically recorded in our review. None of the 343 patients had clinically apparent pancreatitis.

Since July, 1989, we have prospectively studied adults admitted to our unit with acute gastroenteritis. Patients thought to have toxin-mediated food poisoning at the time of admission were excluded from the study protocol, which includes at least two blood cultures and estimation of serum amylase on admission, but does not routinely include sonography. The distribution of causative pathogens is representative of patients admitted to our unit with gastroenteritis[1] and the commonest salmonella isolates were *S enteritidis* (46·5%) and *S typhimurium* (17·2%). None of the patients had clinically apparent pancreatitis. Serum amylase activities (normal range 10–96 IU/l) that were available for 147 of 171 patients are summarised below:

Pathogen	*n*	*Age (years) mean (SD)*	*Serum amylase (IU/l) mean (SD)*
None isolated	63	43·6 (19·5)	37·6 (22·4)
Salmonella	51	37·7 (19·3)	33·5 (18·9)
Campylobacter	22	40·1 (18·4)	32·2 (21·7)
Miscellaneous	11	43·6 (17·1)	30·1 (16·7)
Total	147	41·1 (19·2)	34·8 (20·7)

There was no difference (Kruskal–Wallis) in the mean amylase activities among the salmonella group compared with the campylobacter group, or between the salmonella and campylobacter groups combined compared with all other pathogens. Slightly raised amylase activites were found in only 1 patient with salmonella (110 IU/l) and in 3 with no pathogen isolated (98, 112, and 135 IU/l). None of the 5 bacteraemic salmonella patients had a raised serum amylase.

Our findings contrast with the 62% of patients with salmonella reported by Renner et al and the high frequency of campylobacter isolates reported by others,[2] all of which have been associated with raised amylase and lipase activities. Although cases of severe pancreatitis associated with campylobacter infections have been reported,[3,4] this complication appears to be rare. We agree that an infective cause should be thought of in a patient with abdominal pain, diarrhoea, and hyperamylasaemia, but we question the clinical importance of hyperamylasaemia in the majority of patients with infective gastroenteritis.

S. MURPHY
N. J. BEECHING
S. J. ROGERSON
A. D. HARRIES

Regional Infectious Disease Unit,
Fazakerley Hospital,
Liverpool L9 7AL, UK

1. Felton M, Harries AD, Beeching NJ, Rogerson SJ, Nye FJ. Acute gastroenteritis: the need to remember alternative diagnoses. *Postgrad Med J* 1990; 66: 1037–39.
2. Pitkänen T, Pöntä A, Pettersson T, Kosunen TU. Campylobacter enteritis in 188 hospitalized patients. *Arch Intern Med* 1983; 143: 215–19.
3. Gallagher P, Chadwick P, Jones DM, Turner L. Acute pancreatitis associated with campylobacter infection. *Br J Surg* 1981; 68: 383.
4. de Bois MHW, Shoemaker MC, Van der Werf SDJ, Puylaert JBCM. Pancreatitis associated with *Campylobacter jejuni* infection: diagnosis by ultrasonography. *Br Med J* 1989; 298: 1004.

Healing of cavity wounds with sugar

SIR,—Your April 27 editorial discusses the use of sugar paste as formulated by us. We were surprised by Professor Parish and Professor Witkowski's (June 1, p 1355) dismissal of the use of sugar as a treatment for the healing wound.

The safe and effective application of ordinary granulated sugar to infected wounds has been recorded previously in *The Lancet*.[1,2] We have formulated caster sugar (fine granular sucrose) and icing sugar (powdered sucrose) with polyethylene glycol 400 and hydrogen peroxide into thick and thin pastes.[3] We have shown these pastes to be non-toxic to healing wounds in a controlled trial in the domestic pig.[4] The effects of sugar paste on water activity and bacterial growth in vitro have been investigated.[5] Within wounds, these sugar pastes reduce the available water and this inhibits bacterial growth; however, they still allow granulation tissue to form and